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Case report

Ictal asystole—Late manifestation of partial epilepsy and importance of cardiac pacemaker

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ABSTRACT

Ictal asystole (IA) is a life-threatening complication of epilepsy and is a potential mechanism of sudden unexplained death in epilepsy (SUDEP). This entity has been proven by multiple case reports and small case series. The management of the patients with IA is still in early phase of discussion. We report a patient with medically intractable cryptogenic partial epilepsy for 27 years who presented with new onset drop attacks. During the epilepsy monitoring unit stay he was found to have a left fronto-temporal partial onset seizures which triggered brady-arrhythmia followed by asystole for 20 s. A cardiac pacemaker was implanted and the patient was followed for 2 years. He continued to have simple and complex partial seizures but did not have drop attacks anymore. He still occasionally feels the activation of his pacemaker during simple partial phase of his seizures but the characteristic loss of muscle tone never happened again which made him highly satisfied. Our case demonstrates that IA can even happen decades after the onset of epilepsy. Cardiac pacemaker should be considered in all patients with IA as it prevents ictal falls and possibly SUDEP.

1. Introduction

Heart rate changes secondary to mesial temporal lobe seizures were first described by Jackson and Beevor.[1] Erickson[2] first scientifically studied ictal electrocardiogram (ECG) changes including tachycardia, cardiac arrhythmias, and T-wave flattening resulting from temporal lobe seizures. Correlation of epileptic activity in temporal region with cardiovascular phenomena was further established in later studies by Gastaut,[3] White et al.[4] and Van Buren.[5] Oppenheimer et al.,[6] reported that stimulation of the left anterior insula causes bradycardia and depressor responses whereas stimulation of right insular cortex induces tachycardia and pressor response. This finding has been confirmed by other researchers[7] initially but still is a topic of debate.

In a recent review article,[8] ictal asystole (IA) was seen in 0.27% of all patients with epilepsy who underwent video-EEG monitoring. Among these patients, almost 80% of IA events were seen with temporal lobe seizures and around 20% with extra-temporal lobe seizures, but not in patients with generalized seizures. In the same review, it was recommended to consider long-term video-EEG monitoring in patients with temporal lobe seizures with unexpected collapse and falls late in the course of a typical seizure as this might be the only sign of IA. We present a patient with childhood temporal lobe partial epilepsy with new onset ictal falls and subsequent trauma who was found to have IA during long-term video-EEG monitoring.

2. Case report

A 31-year-old male with history of staring spells lasting from 10 to 30 s since age 3 years. They were effectively treated with phenobarbital for 4 years after which it was tapered off. He continued to have these spells but was not on any medications till age 24 when he was started on phenytoin by a neurologist which was continued for another 6 years. He continued to have these staring spells almost 1–2 times per month. They were associated with oro-buccal automatisms, restlessness, aphasia, picking movements of his clothes and loss of awareness. At age 30, he experienced new type of events which started as his typical seizures but were followed by sudden loss of body tone for almost 15–20 s. At times, these events were followed by brief jerks involving the whole body. He was evaluated by cardiology and

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neurology for syncope. He had a normal cardiac and neurological workup including ECG, transthoracic echocardiogram (TTE), outpatient electroencephalography (EEG), magnetic resonance imaging (MRI) and magnetic resonance angiogram (MRA) of the brain. He was admitted to the hospital in May 2005 for continuous video-EEG monitoring for characterization of these spells.

During his epilepsy monitoring unit stay, three events were captured:

Events #1 and 2 were simple and complex partial seizures respectively with left fronto-temporal rhythmic theta activity with associated bradycardia during event #2.

Event #3: During this event, patient had a sudden behavioral arrest. It was followed by a head jerk, loss of awareness, facial automatism, picking motions of right hand followed by generalized loss of tone. EEG at the onset was obscured by muscle artifact but just after that there was diffuse irregular theta activity which was more prominent in the left fronto-temporal region. Over the next 10 s, this activity built up and became semi-rhythmic. Within the next few seconds, it evolved into diffuse theta/delta activity but remained prominent in the left hemisphere. On the other hand, the ECG showed a drop in heart rate from 108 to 36. It was followed by asystole that lasted 10 s after which he had two isolated rescue beats and again went into asystole for 8 s. It was noteworthy that the ictal discharge preceded the ECG changes by almost 15 s (see EEG clips; Fig. 1). The head jerk coincided with brady-arrhythmia and generalized atonia correlated with the asystole. This proved that the onset of the electrographic seizure was the initial event that led to the patient's cardiac rhythm changes and loss of tone. After the asystole, the EEG showed generalized voltage attenuation and the patient had a few myoclonic jerks before he started to wake up but remained post-ictally confused. This event was considered a complex partial event and was associated with asystole.

Cardiology was consulted and he was taken to the cardiac catheterization lab where a dual chamber cardiac pacemaker was implanted. He was restarted on phenytoin and levetiracetam was added. He was offered further invasive monitoring and epilepsy surgery which the patient refused. At 2 years follow-up, patient was off of phenytoin and was only on levetiracetam. He continued to have complex partial seizures which were less frequent. He denied any syncopal events and the subsequent injuries associated with ictal falls but still occasionally felt activation of his pacemaker with simple partial phase of his seizures. He definitely went into cardiac asystole due to the left fronto-temporal ictal discharge which was life threatening and the decision to place cardiac pacemaker helped to stop drop attacks and improved the quality of his life.

3. Discussion

IA is a rare but potentially life-threatening phenomenon predominantly seen in patients with partial epilepsy. Clinically, attacks of IA are usually associated with loss of muscle tone or brief, arrhythmic, bilateral upper extremity posturing and jerking that is distinct from the rhythmic and more sustained tonic–clonic activity or dystonic posturing typically seen in the context of seizures not complicated by cardiac arrhythmias.[9] In our patient, seizures started at 3 years of age and after 27 years he developed new type of spells for which the outpatient workup was unrevealing. Our case demonstrates that it is not necessary to have IA as an initial presentation as he developed this after almost 27 years. Ictal falls might be the only ictal semiology. Gambardella et al.,[10] presented six patients with temporal lobe drop attacks (TLDA), all of whom underwent temporal resection. Postoperative follow-up of at least 1 year was available in all. TLDA were never the first manifestation but followed the onset of epilepsy after a long delay ranging from 7 to 43 years (mean, 24.4 years). In all these patients, seizures were of unilateral temporal origin. In this paper, none of the patients were diagnosed with IA and authors did not discuss the correlation of these TLDA with this phenomenon. Post-surgically, one of these six patients had no TLDA but experienced sporadic auras like our patient.

It has been reported in multiple case reports and case series that the most common localization of epilepsy in the patients with IA is temporal lobe. Our patient had a non-localizable ictal semiology at the onset, diffuse EEG abnormalities with left fronto-temporal predominance and normal MRI brain. Due to these factors, we cannot confirm the exact epileptic focus in our patient. We intended to perform invasive monitoring but due to patient's refusal for a surgical workup, it was not performed. However, with the information in hand, it seems like the probable onset was in left fronto-temporal region (predominant left fronto-temporal irregular theta at onset and right hand automatisms).

It is an ongoing debate if IA is a potential mechanism for sudden unexpected death in epilepsy (SUDEP). Current hypotheses states that seizures may lead to stimulation of the insula, cingulate cortex, amygdala or hypothalamus, which regulate cardiac function through connections to brainstem and spinal cord nuclei.[6,11,12] Scott and Fish[13] reviewed the data and concluded that cardiac and respiratory parameters during partial seizures showed central apnea in 39% patients. It is probable that sudden death during seizures is due to the interaction of both cardiac and respiratory irregularities. Rugg-Gun et al.[14] used implantable loop recorders to get ECG in patients during typical seizures and found that 4 out of 19 patients had bradycardia or periods of IA. Three out of these four had potentially fatal asystoles. These authors concluded that the clinical characteristics of patients with peri-ictal cardiac abnormalities are closely similar to those at greatest risk of SUDEP. In another recent study,[15] cardiac pacemaker was recommended as it prevented ictal syncope and subsequent trauma in one patient.

Ghearing et al.[9] presented long-term results after pacemaker placement for patients with IA. One out of seven patients with pacemaker reported a seizure-related fall in a mean follow-up period of 27 months. Before implantation, all these patients experienced falls and unconsciousness. It is clear with the present knowledge that cardiac pacemakers can decrease the morbidity however it is not evident with present level of understanding if there is any mortality benefit as all the reported cases of IA were spontaneously reversible. One recent study[16] proposed that mechanism of IA is similar to vasovagal asystole (VVA) which is considered to be due to increased vagal tone. In multiple studies it has been shown that VVA is reversible and there is no need of a cardiac pacemaker. The authors have proposed that patients with IA may escape permanent cardiac arrest without being threatened by SUDEP through similar compensatory mechanism as seen in VVA. However with the current data, it is better to consider cardiac pacemaker in patients with IA until we reach a final conclusion regarding the importance and utility of this modality of treatment in these patients.

Our patient was started on phenytoin at the age of 24, almost 6 years before he developed these new types of spells. It is possible that phenytoin might have contributed to this asystole as it has been implicated in causing arrhythmias.[17] However, at the time of the monitoring, phenytoin was stopped and at the time of his third event, his blood level of phenytoin was undetectable. It is more likely that the late onset of the ictal asystole resulted from establishment of new pathways from the

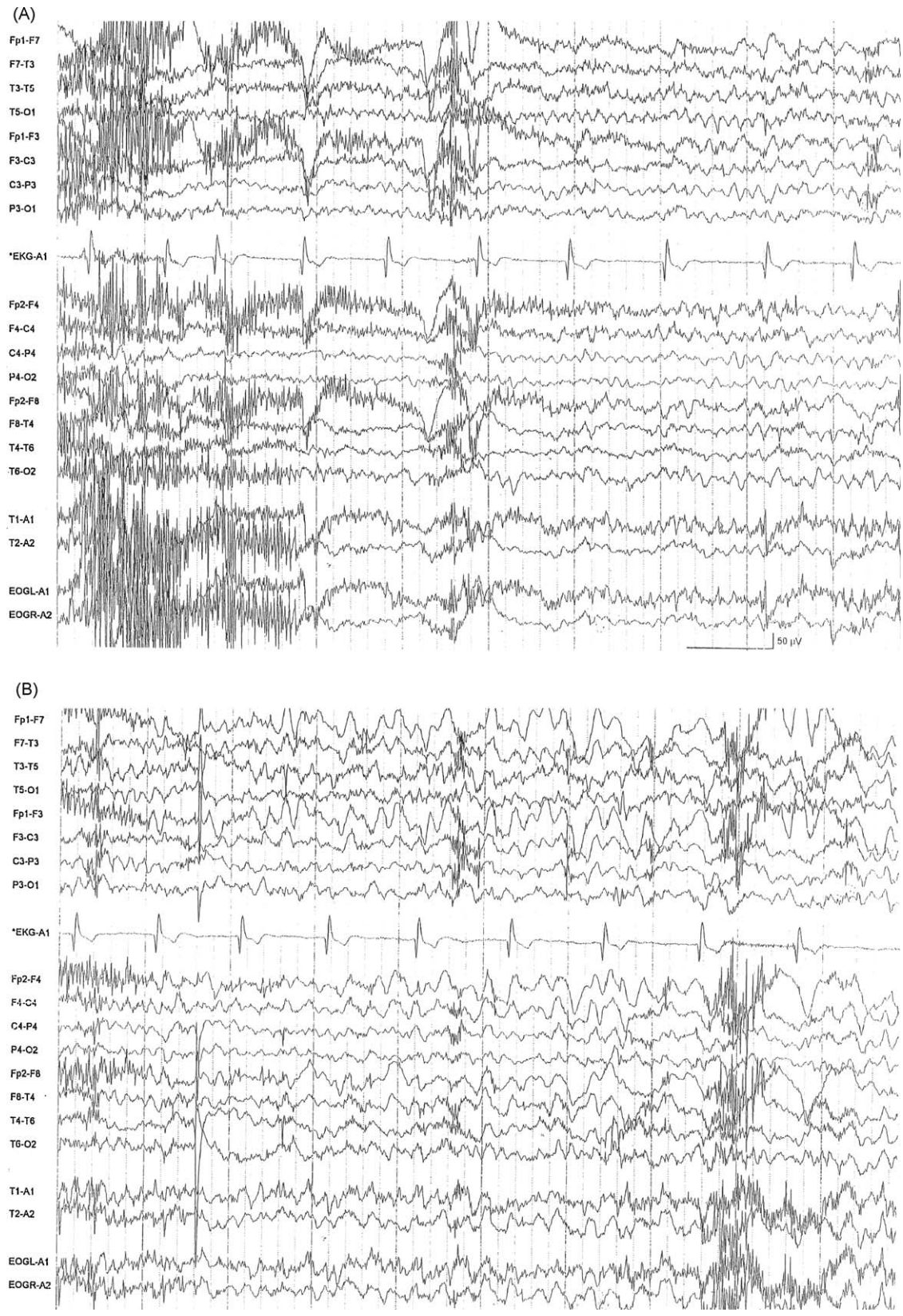

Fig. 1. (A) Onset with bilateral fronto-temporal quasi-rhythmic activity, left > right. (B) Diffuse rhythmic theta/delta activity, more prominent in the left hemisphere. (C) Brady-arrhythmia leading to asystole. (D) Ictal asystole lasting for ~15 s—EEG with generalized attenuation. (E) Ictal asystole ends here with EEG still showing generalized attenuation.

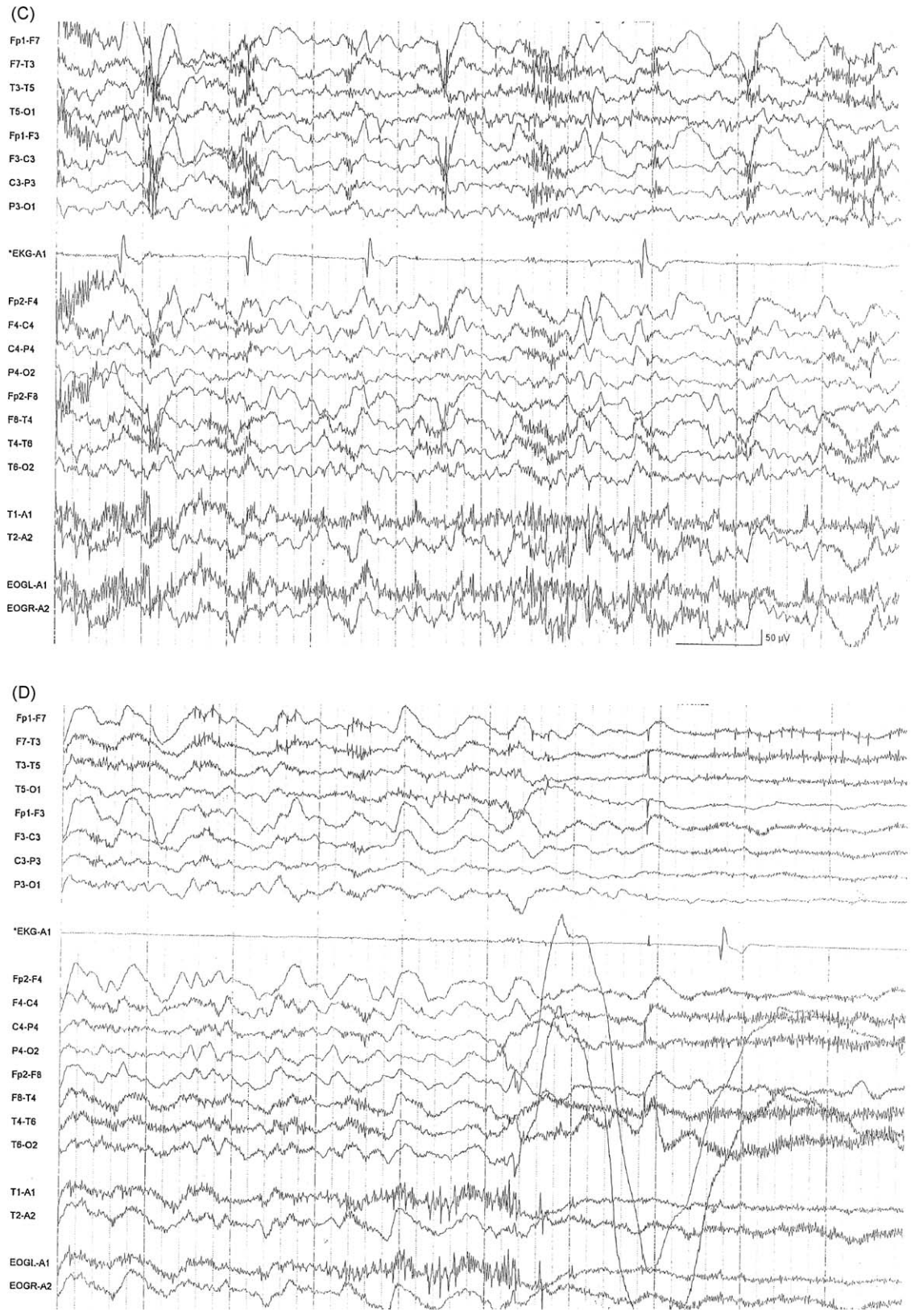

Fig. 1. (*Continued*).

epileptogenic zone to the insular cortex, resulting in asystole and thereby a new behavioral symptom as a result of the asystole, at a later date. Another point that goes in favor of the fact that IA was not due to phenytoin was that the patient, even a year after stopping it, continued to feel activation of his pacemaker with simple partial phase of his seizures. Further, in another study, phenytoin was considered not to be implicated in causing arrhythmias.[18]

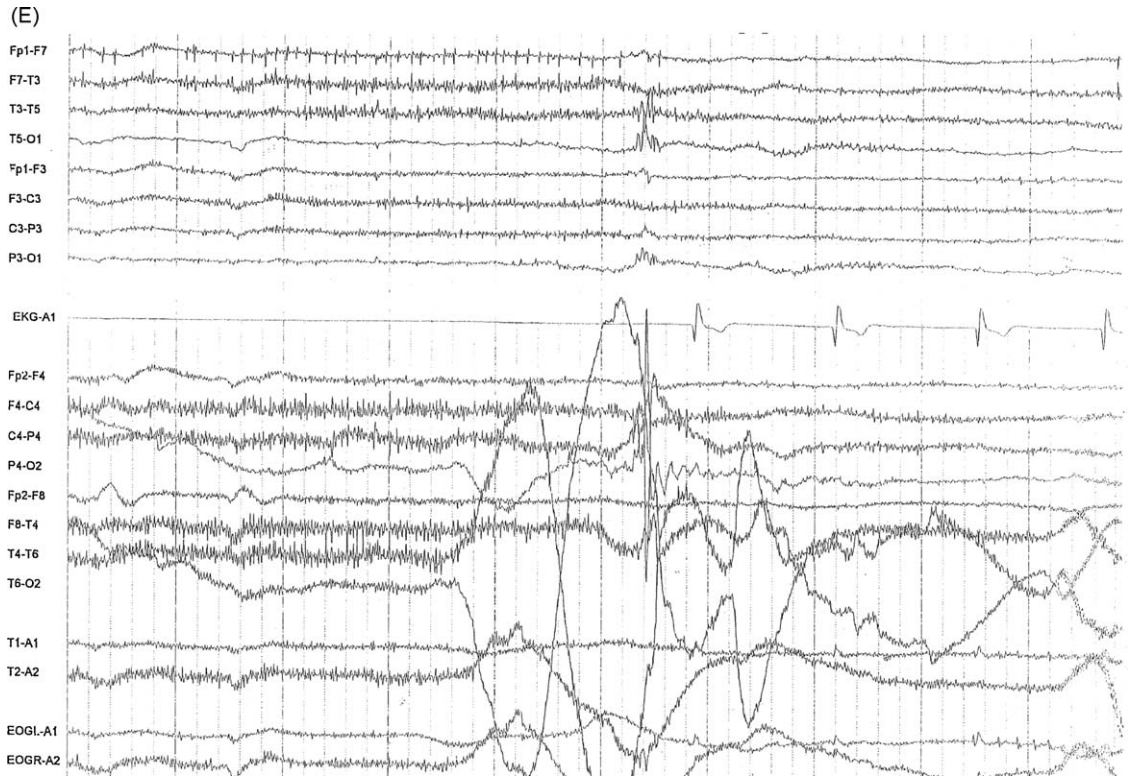

Fig. 1. (*Continued*).

4. Conclusions

1. New onset of syncope with falls in patients with temporal lobe epilepsy should make us consider the possibility of IA.
2. IA can happen after many years of epilepsy and may not be the initial presentation.
3. We propose the fronto-temporal region to be the probable localization of IA, however it is unclear to confirm the lateralization.
4. Continuous video-EEG monitoring may be the only tool to diagnose IA.
5. Cardiac pacemaker should be considered in patients with IA associated with falls as it can decrease the morbidity and probably the mortality, however it has to be further investigated.

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